

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 46/AJW	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/GB2004/004216	International filing date (day/month/year) 05/10/2004	(Earliest) Priority Date (day/month/year) 10/10/2003
Applicant  VERNALIS (CAMBRIDGE) LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

**4. With regard to the title,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

**5. With regard to the abstract,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. With regard to the drawings,**

- a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB2004/004216

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61K31/4365 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 2004/054505 A (KOLODZIEJ STEPHEN A ; VERNIER WILLIAM F (US); LEE LEN F (US); PHARMACI) 1 July 2004 (2004-07-01) page 123, line 26 page 259, line 20 claim 23	1-15
X	DD 275 688 A (UNIV LEIPZIG) 31 January 1990 (1990-01-31) the whole document	1-15
X	WO 93/13664 A (SCHERING AGROCHEMICALS LTD) 22 July 1993 (1993-07-22) example 50	15
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

21 January 2005

Date of mailing of the international search report

28/01/2005

Name and mailing address of the ISA

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Authorized officer

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB2004/004216

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SHERIF S M ET AL: "BETA-ENAMINONITRILES IN HETEROCYCLIC SYNTHESIS: A NOVEL ONE-POT SYNTHESIS OF THIOPHENES AND THEIR FUSED DERIVATIVES" JOURNAL OF CHEMICAL RESEARCH. SYNOPSES, LONDON, GB, 1996, pages 356-357, XP001166932 ISSN: 0308-2342 the whole document	15
X	LEISTNER SIEGFRIED ET AL: "1,3-Bis(pyridin-2-ylthio)propan-2-ones, Bis(thieno(2,-3-b)pyridin-2-y l)ketones and 5H-Bispyrido(3,2':4,5)thieno(2,3-b:2',3'-e )pyridin-11-ones" ARCHIV DER PHARMAZIE (WEINHEIM), vol. 326, no. 12, 1993, pages 959-961, XP009042878 ISSN: 0365-6233 page 960	15
A	WO 03/037860 A (KASIBHATLA SRINIVAS RAO ; ZHANG LIN (US); BOEHM MARCUS F (US); FAN JUN) 8 May 2003 (2003-05-08) the whole document	1-15

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB2004/004216

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 12-14 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB2004/004216

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2004054505	A	01-07-2004	WO 2004054505 A2	01-07-2004
			US 2004127519 A1	01-07-2004
			US 2004127511 A1	01-07-2004
DD 275688	A	31-01-1990	DD 275688 A1	31-01-1990
WO 9313664	A	22-07-1993	AU 3262593 A	03-08-1993
			CN 1076697 A	29-09-1993
			WO 9313664 A2	22-07-1993
WO 03037860	A	08-05-2003	CA 2464031 A1	08-05-2003
			EP 1440072 A2	28-07-2004
			WO 03037860 A2	08-05-2003

# PATENT COOPERATION . REATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

To:

see form PCT/ISA/220

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/GB2004/004216

International filing date (day/month/year)  
05.10.2004

Priority date (day/month/year)  
10.10.2003

International Patent Classification (IPC) or both national classification and IPC  
A61K31/4365, A61P35/00

Applicant  
VERNALIS (CAMBRIDGE) LIMITED

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/GB2004/004216

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/GB2004/004216

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**Box No. II    Priority**

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1. ☐ The following document has not been furnished:
- ☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
  - ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).
- Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. ☒ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
4. Additional observations, if necessary:



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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 1-14 (in part)

because:

- ☒ the said international application, or the said claims Nos. 12-14 (I.A. only) relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-12 (in part) are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- |                            |  |
|----------------------------|--|
| the written form           | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/GB2004/004216

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**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-15
Inventive step (IS)	Yes: Claims	
	No: Claims	1-15
Industrial applicability (IA)	Yes: Claims	1-11, 15
	No: Claims	12-14

2. Citations and explanations

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 12-14 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

The reference to a mechanism, the "inhibition of HSP90" (second medical use claims 1-11 and method of treatment claim 12), is not considered a clear definition of the disease (Clarity, Art. 6 PCT). The medical use claims shall refer to a real, defined therapeutical application, such as those diseases listed in claims 13 and 14.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: WO 2004/054505 A (KOLODZIEJ STEPHEN A ; VERNIER WILLIAM F (US); LEE LEN F (US); PHARMACI) 1 July 2004 (2004-07-01)
- D2: DD 275 688 A (UNIV LEIPZIG) 31 January 1990 (1990-01-31)
- D3: WO 93/13664 A (SCHERING AGROCHEMICALS LTD) 22 July 1993 (1993-07-22)
- D4: SHERIF S M ET AL: "BETA-ENAMINONITRILES IN HETEROCYCLIC SYNTHESIS: A NOVEL ONE-POT SYNTHESIS OF THIOPHENES AND THEIR FUSED DERIVATIVES" JOURNAL OF CHEMICAL RESEARCH. SYNOPSES, LONDON, GB, 1996, pages 356-357, XP001166932 ISSN: 0308-2342
- D5: LEISTNER SIEGFRIED ET AL: "1,3-Bis(pyridin-2-ylthio)propan-2-ones, Bis(thieno(2,-3-b)pyridin-2-yl)ketones and 5H-Bispyrido(3,2':4,5)thieno(2,3-b:2',3'-e)pyridin-11-ones" ARCHIV DER PHARMAZIE (WEINHEIM), vol. 326, no. 12, 1993, pages 959-961, XP009042878 ISSN: 0365-6233
- D6: WO 03/037860 A (KASIBHATLA SRINIVAS RAO ; ZHANG LIN (US); BOEHM MARCUS F (US); FAN JUN) 8 May 2003 (2003-05-08)

**Novelty - Article 33(2) PCT**

D2 (DD275688) discloses compounds of formula (I) that appear to be of pharmaceutical use (abstract). Although there are no explicit therapeutic indications mentioned in D2, it is considered novelty-destroying for the independent claims (second medical use claim 1, method of treatment claim 12, composition claim 15), having regard to the unclear definition of the claimed therapeutic effect (cf. Item III above).

In D5 (Leistner et al.), compound 3d appears to fall under formula (I). D3

(WO9313664) discloses cyclohexyl 3,6-diamino-5-cyano-4-methylthiothienot2,3-b] pyridine- 2-carboxylate (example 50). Also the publication by Sherif et al. (D4) discloses compounds falling under formula (I).

It should be pointed out that the intended use, "pharmaceutical or veterinary", is not a limiting feature in product claim 15. Hence, any composition of a compound of formula (I) destroys novelty for such a claim.

The disclosure in the above documents is therefore considered novelty-destroying for the subject-matter of claim 15.

**Industrial Applicability - Article 33(4) PCT**

For the assessment of the present claims 1-14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.